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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
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| 10/060,830 | 01/30/2002 | Yizhong Gu | PB0169 | 3442 |

7590 07/29/2003

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| EXAMINER | |
|---|---|
| SWOPE, SHERIDAN | |

| ART UNIT | PAPER NUMBER |
|---|---|
| 1652 | 13 |

DATE MAILED: 07/29/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

| .Office Action Summary | Application No. | Applicant(s) | |
|---|---|---|---|
| | 10/060,830 | GU, Y. ET AL | |
| | Examiner | Art Unit | |
| | Sheridan L. Swope | 1652 | |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☐ Responsive to communication(s) filed on *11 June 2003* .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) *1 and 3-49* is/are pending in the application.

4a) Of the above claim(s) *13-31, 34-38, and 40-47* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,3-12,32,33,39,48 and 49* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

**Application Papers**

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

**Priority under 35 U.S.C. §§ 119 and 120**

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

**Attachment(s)**

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

## DETAILED ACTION

Applicant's response, on June 11, 2003, Paper No. 12, is acknowledged. It is acknowledged that applicants have amended Claims 1, 4, and 11, cancelled Claim 2, withdrawn Claims 13-31, 34-38, and 40-47, and added Claims 48 and 49. Claims 1, 3-12, 32, 33, 39, are hereby reconsidered, while Claims 48, and 48 are hereby considered.

### *Claim Rejections - 35 USC § 101*

Rejection of Claims 1, 3-12, 32, 33, and 39 under 35 U.S.C. 101 because the claimed invention lacks patentable utility, as described in the prior action, is maintained. Applicants argue that the claimed nucleic acids can be used to encode proteins which, because of having an LCCL domain, have potential (emphasis added by the examiner) therapeutic as well as diagnostic roles in neurological and developmental disorders and diseases involving cell- cell adhesion. Applicant's response also states that the nucleic acids have utility as PCR primers/probes, can be used in microarrays, and in vectors for transforming host cells which can be used to produce the encoded polypeptides. These arguments are not found to be persuasive.

The recitation of a role in neurological and developmental disorders and diseases involving cell- cell adhesion does not constitute a specific utility, as many proteins are involved in developmental disorders and diseases involving cell- cell adhesion. Furthermore, the presence of an LCCL domain in the proteins encoded by the recited polynucleotides is not sufficient to conclude that said polynucleotides or proteins can be used to treat or diagnose any specific disease. The use of the recited polynucleotides as PCR primers/probes, in microarrays, and to produce the encoded polypeptides are applications which would apply to every member of a general class of materials and/or is a use only for further research to determine a use for the

recited polynucleotides. As such, these asserted utilities are not specific (for those applicable to all polynucleotides) or not substantial because the use of said polynucleotides and the encoded proteins as therapeutics or in diagnostics is only potential and not in currently available in practical form. Therefore, rejection of Claims 1, 3-12, 32, 33, and 39 under 35 U.S.C. 101 because the claimed invention lacks patentable utility is maintained.

***Claim Rejections - 35 USC § 112-First Paragraph***

Rejection of Claims 1, 3-12, 32, 33, and 39 under 35 U.S.C. 112, first paragraph because the claimed invention is not supported by either a convincing asserted utility or a well established utility and, therefore, one skilled in the art clearly would not know how to use the claimed invention is maintained.

Even if applicants address the 35 U.S.C. 101 rejection above and show a specific, substantial and credible utility for nucleic acids encoding SEQ ID NO: 2 and SEQ ID NO: 1113, the following rejection under 35 U.S.C. 112 applies. Rejection of Claims 1, 3-12, 32, 33, and 39 under 35 U.S.C. 112, first paragraph, for lack of enablement is maintained, while new Claims 48 and 49 are hereby rejected under 35 U.S.C. 112, first paragraph. Applicants argue that amendment of Claim 1 to delete the phrase "with conservative amino acid substitutions" and limitation of Claim 1 to the sequences or complete complement sequences of SEQ ID NO: 2 or SEQ ID NO: 1113 or SEQ ID NO: 3 or SEQ ID NO: 1114, or to sequences at least 90% identical over comes the rejection of the prior action. This argument is not found to be persuasive. It is acknowledged that applicants have limited the scope of the invention recited by Claim 1. However, the scope of the amended Claim 1 is not enabled for the following reasons. While the specification is enabling for SEQ ID NO: 2 and SEQ ID NO: 1113, it does not reasonably

provide enablement for any nucleic acid encoding a polypeptide comprising 90%, 95%, or 99% identity with SEQ ID NO: 2 or SEQ ID NO: 1113. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

Claim 1 is so broad as to encompass any polynucleotide sequence that encodes a protein having 90% identity with SEQ ID NO: 2 or SEQ ID NO: 1113. Claim 48 is so broad as to encompass any polynucleotide sequence that encodes a protein having 95% identity with SEQ ID NO: 2 or SEQ ID NO: 1113. Claim 49 is so broad as to encompass any polynucleotide sequence that encodes a protein having 99% identity with SEQ ID NO: 2 or SEQ ID NO: 1113. The scope of these claims is not commensurate with the enablement provided by the disclosure with regard to the extremely large number of polynucleotides broadly encompassed by the claim. Since the amino acid sequence of a protein determines its structural and functional properties, predictability of which changes can be tolerated in a protein's amino acid sequence and obtain the desired activity requires a knowledge of and guidance with regard to which amino acids in the protein's sequence, if any, are tolerant of modification and which are conserved (i.e. expectedly intolerant to modification), and detailed knowledge of the ways in which the protein's structure relates to its function.

While recombinant and mutagenesis techniques are known, it is not routine in the art to screen for multiple substitutions or multiple modifications, as encompassed by the instant claims, and the positions within a protein's sequence where amino acid modifications can be made with a reasonable expectation of success in obtaining the desired activity/utility are limited in any protein and the results of such modifications are unpredictable. In addition, one skilled in the art

would expect any tolerance to modification for a given protein to diminish with each further and additional modification, e.g. multiple substitutions.

The specification does not support the broad scope of the Claim 1 which, encompasses any polynucleotide sequence that encodes a protein having 90% identity with SEQ ID NO: 2 or SEQ ID NO: 1113. The specification does not support the broad scope of the Claim 48 which, encompasses any polynucleotide sequence that encodes a protein having 95% identity with SEQ ID NO: 2 or SEQ ID NO: 1113. The specification does not support the broad scope of the Claim 49 which, encompasses any polynucleotide sequence that encodes a protein having 99% identity with SEQ ID NO: 2 or SEQ ID NO: 1113. The specification does not support the broad scope of Claims 1, 48, and 49 because the specification does not establish: (A) the desired activity for any polypeptides having 90%, 95%, or 99% identity with SEQ ID NO: 2 or SEQ ID NO: 1113; (B) regions of the protein structure which may be modified without effecting the role in the desired activity; (C) the general tolerance of the desired activity to modification and extent of such tolerance; (D) a rational and predictable scheme for modifying any residues with an expectation of obtaining the desired biological function; and (E) the specification provides insufficient guidance as to which of the essentially infinite possible choices is likely to be successful.

Since Claims 2-12, 32, 33, and 39 further recite probes, microarrays, vectors, host cells methods of expressing the nucleic acids of Claim 1, and compositions comprising the nucleic acids of Claim 1, Claims 2-12, 32, 33, and 39 are also rejected under 35 U.S.C. 112 first paragraph due to lack of enablement for the same reasons discussed above.

Thus, applicants have not provided sufficient guidance to enable one of ordinary skill in the art to make the claimed invention in a manner reasonably correlated with the scope of the

claims broadly including any number of polynucleotides encoding any polypeptide with an enormous number of amino acid modifications of the proteins of SEQ ID NO: 3 and SEQ ID NO: 1114 wherein said polypeptides have an undisclosed activity. The scope of the claims must bear a reasonable correlation with the scope of enablement (In re Fisher, 166 USPQ 19 24 (CCPA 1970)). Without sufficient guidance, determination of the identity of sequences having the desired biological characteristics is unpredictable and the experimentation left to those skilled in the art is unnecessarily, and improperly, extensive and undue. See In re Wands 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir, 1988).

Rejection of Claims 1, 3-12, 32, 33, and 39 under 35 U.S.C. 112, first paragraph, for lack of written description, is also maintained, while new Claims 48 and 49 are hereby rejected under 35 U.S.C. 112, first paragraph for lack of written description. Applicants argue that, one of ordinary skill in the art can clearly determine that Applicants were in possession of the invention of Claim 1, as amended. This argument is not found to be persuasive. As described above for lack of enablement, it is acknowledged that Applicants have limited the scope in new Claim 1. However, the scope of new Claim 1 is such that it contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. Claim 1 is now directed to a genus of DNA molecules encoding polypeptides having 90% identity with SEQ ID NO: 2 or SEQ ID NO: 1113. Furthermore, Claims 48 and 49 are directed to a genus of DNA molecules encoding polypeptides having 95% or 99% identity, respectively, with SEQ ID NO: 2 or SEQ ID NO: 1113. The specification does not contain any disclosure of the function of all DNA sequences encoding polypeptides having 90%, 95%, or

99% identity with SEQ ID NO: 2 or SEQ ID NO: 1113. The genus of polynucleotides that comprise these above cDNA molecules is a large variable genus with the potentiality of encoding many different proteins. Therefore, many functionally unrelated DNAs are encompassed within the scope of these claims, including partial DNA sequences. The specification does not disclose the function of any species of the claimed genus and, thus, does not put one of skill in the art in possession of the attributes and features of any species within the claimed genus. Therefore, one skilled in the art cannot reasonably conclude that the applicant had possession of the claimed invention at the time the instant application was filed.

Applicant is referred to the revised guidelines concerning compliance with the written description requirement of U.S.C. 112, first paragraph, published in the Official Gazette and also available at www.uspto.gov.

## NEW ISSUES

### *Claim Rejections - 35 USC § 101*

35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claims 48 and 49 are rejected under 35 U.S.C. 101 for the same reasons described above for rejection of Claims 1, 3-12, 32, 33, and 39.

### *Claim Rejections - 35 USC § 112-First Paragraph*

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 48 and 49 are also rejected under 35 U.S.C. 112, first paragraph. Specifically, since the claimed invention is not supported by either a credible asserted utility or a well established utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention.

Claims 48 and 49 are further rejected under 35 U.S.C. 112, first paragraph for lack of enablement and written description as described above (pg3, prgX-pg7, prg1).

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Sheridan L. Swope whose telephone number is 703-305-1696. The examiner can normally be reached on M-F; 9:30-7 EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ponnathapura Achutamurthy can be reached on 703-308-3804. The fax phone

numbers for the organization where this application or proceeding is assigned are 703-305-3014 for regular communications and 703-872-9307 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

Sheridan L. Swope, Ph.D.